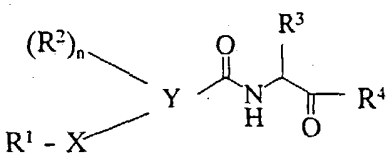
Novel heterocyclically substituted amides, their preparation and use

We claim:

1. An amide of the general formula I



and its tautomeric and isomeric forms, possible enantiomeric and diastereomeric forms, as well as possible physiologically tolerable salts, in which the variables have the following meanings:

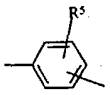
R^1 can be phenyl, naphthyl, quinolyl, pyridyl, pyrimidyl, pyrazyl [sic], pyridazyl, imidazolyl, thiazole, quinazyl, isoquinolyl, quinazyl [sic], quinoxalyl, thienyl, benzothienyl, benzofuranyl, furanyl, and indolyl, where the rings can be additionally substituted by up to 3 radicals R^5,

R^2 is chlorine, bromine, fluorine, C_1-C_6-alkyl, C_1-C_6-alkenyl, C_1-C_6-alkynyl, C_1-C_6-alkylphenyl, C_1-C_6-alkenylphenyl, C_1-C_6-alkynylphenyl, phenyl, NHCO-C_1-C_4-alkyl, $NHSO_2$-C_1-C_4-alkyl, -NHCOphenyl [sic], -NHCO-naphthyl, NO_2, -O-C_1-C_4-alkyl and NH_2, where the aromatic rings can additionally carry one or two radicals R^5 and two radicals R^2 together can also be a chain -CH=CH-CH=CH- and thus form a fused benzo ring, which for its part can be substituted by one R^5 and

R^3 is -C_1-C_6-alkyl, which is branched or unbranched, and which can additionally carry an S-CH_3 radical or a phenyl, cyclohexyl, cycloheptyl, cyclopentyl, indolyl, pyridyl or naphthyl ring which for its part is substituted by by [sic] at most two radicals R^5, where R^5 is hydrogen, C_1-C_4-alkyl, which is branched or unbranched, -O-C_1-C_4-alkyl, OH, Cl, F, Br, I, CF_3, NO_2, NH_2, CN, COOH, COO-C_1-C_4-alkyl, -NHCO-C_1-C_4-alkyl, -NHCO-phenyl, $-NHSO_2$-C_1-C_4-alkyl,

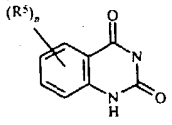
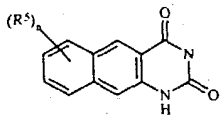
$-NHSO_2$-phenyl, $-SO_2-C_1-C_4$-alkyl, $-(CH_2)_n-NR^{12}R^{13}$ and $-SO_2$-phenyl,

X is a bond, $-(CH_2)_m-$, $-(CH_2)_m-O-(CH_2)_o-$, $-(CH_2)_o-S-(CH2)_m-$ [sic], $-(CH_2)_o-SO-(CH_2)_m-$, $-(CH_2)_o-SO_2-(CH_2)_m-$, $-CH=CH-$, $-C\equiv C-$, $-CO-CH=CH-$, $-(CH_2)_o-CO-(CH_2)_m-$, $-(CH_2)_m-NHCO-(CH_2)_o-$, $-(CH_2)_m-CONH-(CH_2)_o-$, $-(CH_2)_m-NHSO_2-(CH_2)_o-$, $-NH-CO-CH=CH-$, $-(CH_2)_m-SO_2NH-(CH_2)_o-$, $-CH=CH-CONH-$ and



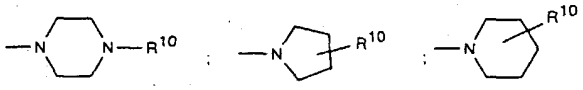
and in the case of CH=CH double bonds can be either the E or the Z form and

R^1-X together are also

 and  and

Y is an unsaturated heterocyclic ring such as pyridine, pyrimidine, pyrazine, imidazole and thiazole and

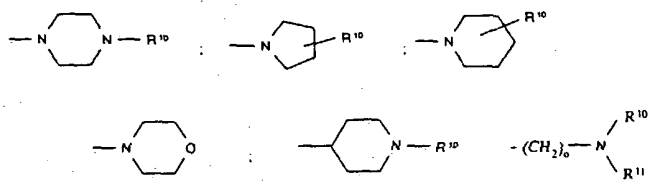
R^4 is hydrogen, $COOR^6$ and CO-Z, in which Z is NR^7R^8, and is



R^6 is hydrogen, C_1-C_6-alkyl, which is linear or branched, and which can be substituted by a phenyl ring which itself can additionally be substituted by one or two radicals R^9, and

R^7 is hydrogen, C_1-C_6-alkyl, which is branched and unbranched, and

R^8 is hydrogen, C_1-C_6-alkyl, which is branched or unbranched which can additionally be substituted by a phenyl ring which can additionally carry a radical R^9, and by



and

R^9 can be hydrogen, C_1-C_4-alkyl, which is branched or unbranched, -O-C_1-C_4-alkyl, OH, Cl, F, Br, I, CF_3, NO_2, NH_2, CN, COOH, COO-C_1-C_4-alkyl, -NHCO-C_1-C_4-alkyl, -NHCO-phenyl, -$NHSO_2$-C_1-C_4-alkyl, -$NHSO_2$-phenyl, -SO_2-C_1-C_4-alkyl and -SO_2-phenyl

R^{10} is hydrogen, C_1-C_6-alkyl, which is linear or branched, and which can be substituted by a phenyl ring which itself can additionally be substituted by one or two radicals R^9, and

R^{11} is hydrogen, C_1-C_6-alkyl, which is linear or branched, and which can be substituted by a phenyl ring which itself can additionally be substituted by one or two radicals R^9, and

n is a number 0, 1 or 2, and

m,o independently of one another is a numeral 0, 1, 2, 3 or 4.

2. An amide of the formula I as claimed in claim 1, where

R^3 is benzyl, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$ and

Y is pyridine and

R^4 is $CO-NR^7NR^8$ and

R^7 is hydrogen

R^8 is CH_2CH_2, $CH_2CH_2CH_2$, $CH_2CH_2CH_2CH_2$ and

R^9 is hydrogen and

n is 0 and 1 and

all remaining variables have the same meanings as in claim 1.

3. An amide of the formula I as claimed in claim 1, where

R^3 is benzyl, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$ and

Y is pyridine and

R^4 is hydrogen and

R^9 is hydrogen

n is 0 and 1 and

all remaining variables have the same meanings as in claim 1.

4. An amide of the formula I as claimed in claim 1, where

R^3 is benzyl, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$ and

Y is imidazole and thiazole and

R^4 is $CO-NR^7NR^8$ and

R^7 is hydrogen

R^8 is CH_2CH_2, $CH_2CH_2CH_2$, $CH_2CH_2CH_2CH_2$ and

R^9 is hydrogen and

n is 0 and 1 and

all remaining variables have the same meanings as in claim 1.

5. An amide of the formula I as claimed in claim 1, where

R^3 is benzyl, CH_2-pyridine, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$ and

Y is imidazole and thiazole and

R^4 is hydrogen and

R^9 is hydrogen and

n is 0 and 1 and

all remaining variables have the same meanings as in claim 1.

6. The use of amides of the formula I as claimed in claim [sic] 1-5 for the treatment of diseases.

7. The use of amides of the formula I as claimed in claim [sic] 1-5 as inhibitors of cysteine proteases.

8. The use as claimed in claim 6 as inhibitors of cysteine proteases such as calpains and cathepsins, in particular calpains I and II and cathepsins B and L.

9. The use of amides of the formula I as claimed in claim [sic] 1-5 for the production as [sic] pharmaceuticals for the treatment of diseases in which increased calpain activity occurs.

10. The use of amides of the formula I as claimed in claim [sic] 1-5 for the production of pharmaceuticals for the treatment of neurodegenerative diseases and neuronal damage.

11. The use as claimed in claim 9 for the treatment of those neurodegenerative diseases and that neuronal damage which is caused by ischemia, trauma or mass hemorrhages.

12. The use as claimed in claim 10 for the treatment of cerebral stroke and craniocerebral trauma.

13. The use as claimed in claim 10 for the treatment of Alzheimer's disease and Huntington's disease.

14. The use as claimed in claim 10 for the treatment of epilepsy.

15. The use of the compounds of the formula I as claimed in claim [sic] 1-5 for the production of pharmaceuticals and treatment of damage to the heart after cardiac ischemias, reperfusion damage after vascular occlusion, damage to the kidneys after renal ischemias, skeletal muscular damage, muscular dystrophies, damage which results due to proliferation of the smooth muscle cells, coronary vasospasm, cerebral vasospasm, cataracts of the eyes and restenosis of the blood vessels after angioplasty.

16. The use of the amides of the formula I as claimed in claim [sic] 1-5 for the production of pharmaceuticals for treating tumors and metastasis thereof.

17. The use of the amides of the formula I as claimed in claim [sic] 1-5 for the production of pharmaceuticals for treating diseases in which increased interleukin-1 levels occur.

18. The use of the amides as claimed in claim [sic] 1-5 for treating immunological diseases such as inflammations and rheumatic disorders.

19. A pharmaceutical preparation for oral, parenteral and intraperitoneal use, comprising per individual dose, in addition to the customary pharmaceutical auxiliaries, at least of [sic] one amide I as claimed in claim [sic] 1-5.